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OM protein - protein search, using sw model

Run on: September 2, 2004, 13:40:11 ; Search time 39.75 Seconds
 (without alignments)
 2345.677 Million cell updates/sec

Title: US-09-717-789b-12
 Perfect score: 1755
 Sequence: 1 MALVNLVHGITSKQWIO.....VDPAPLRPLNWSRLVGRSW 330

Scoring table: BLOSUM62
 Gapop 10.0 , Gapext 0.5

Searched: 1586107 seqs, 282547505 residues

Total number of hits satisfying chosen parameters: 1586107

Minimum DB seq length: 0
 Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
 Maximum Match 100%
 Listing first 45 summaries

Database : A_Geneseq_29Jan04:*

- 1: Geneseq1980s:*
- 2: Geneseq1990s:*
- 3: Geneseq2000s:*
- 4: Geneseq2001s:*
- 5: Geneseq2002s:*
- 6: Geneseq2003as:*
- 7: Geneseq2003bs:*
- 8: Geneseq2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	1755	100.0	330	3	AAY58163
2	1755	100.0	330	5	AAU11408
3	1755	100.0	550	3	AAY58164
4	1755	100.0	550	5	AAU11409
5	1721	98.1	390	3	AAY58158
6	1721	98.1	390	5	AAU11403
7	1721	98.1	610	3	AAY58159
8	1721	98.1	610	4	AAU11404
9	1721	98.1	610	5	AAU11404
10	1721	98.1	610	5	AAE22887
11	1721	98.1	610	5	AAE28644
12	1721	98.1	610	5	AAE26940
13	1721	98.1	610	6	ABU64760
14	1721	98.1	610	6	ABU64760
15	1721	98.1	610	6	ABR43398
16	1169	66.6	399	2	AAW46310
17	1169	66.6	399	6	ABG73937
18	1169	66.6	623	2	AAW46307
19	1169	66.6	623	2	AAW46312
20	1169	66.6	623	4	AAU97712
21	1169	66.6	623	5	AAE28636
22	1169	66.6	623	5	AAE26932
23	1169	66.6	623	6	ABU64857
24	1169	66.6	623	6	ABU64752
25	1169	66.6	623	6	ABG73939

ALIGNMENTS

RESULT 1
 AAY58163
 ID AAY58163 standard; protein; 330 AA.
 XX
 AC AAY58163;
 XX
 DT 07-MAR-2000 (first entry)
 XX
 DE Adeno associated virus AAV5 Rep40 protein.
 XX
 KW Adeno associated virus; AAV5; AAV2; inverted terminal repeat; ITR;
 KW promoter; Rep protein; capsid protein; regulation; transcription;
 KW replication; chromosomal integration; tissue tropism; cellular receptor;
 KW gene therapy; neutralising antibody; erythroid progenitor cell;
 KW transduction; cancer; genetic disease; Rep40.
 XX
 OS Adeno-associated virus 5.
 XX
 PN WO9961601-A2.
 XX
 PD 02-DEC-1999.
 XX
 PF 28-MAY-1999; 99WO-USO11958.
 XX
 PR 28-MAY-1998; 98US-0087029P.
 XX
 PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
 XX
 PI Chiorini JA, Kotin RM;
 XX
 DR WPI; 2000-062707/05.
 DR N-PSDB; AAZ49215.
 XX
 PT Adeno-associated virus 5 based vectors and particles, useful for gene therapy.
 XX
 Claim 16; Page 86; 91pp; English.
 CC This sequence represents the Rep40 protein of adeno associated virus type 5 (AAV5). The invention relates to vectors comprising a pair of AAV5 inverted terminal repeats (ITRs) with a promoter between the ITRs. The vector may comprise the viral genome, or subregions thereof, including sequences encoding Rep proteins and capsid proteins, and is encapsidated in an AAV5 particle. The non-structural Rep proteins, Rep40 (AAY58163), Rep52 (AAY58168), Rep68 (AAY58164) and Rep78 (AAY58159) are involved in regulation of replication and transcription, in addition to the production of progeny genomes. Rep68 and Rep78 are also associated with the stable integration of the viral genome into human chromosomes. The

Abg73934 Adeno-ass
 Abx43390 Adeno-ass
 Aay97713 Rep78 pro
 Aae22880 Adeno-ass
 Aae28637 Adeno-ass
 Aae26933 Adeno-ass
 Abu64858 Rep78 pro
 Abu64753 Adeno-ass
 Abx43391 Adeno-ass
 Aab59850 AAV3B Rep
 Aaw46309 AAV4 Rep
 Abg73936 Adeno-ass
 Aaw46311 AAV4 Rep
 Abg73938 Adeno-ass
 Aay97714 Nonstruct
 Aab59849 AAV3A Rep
 Aae22881 Adeno-ass
 Aae28638 Adeno-ass
 Aae26934 Adeno ass
 Abu64859 Nonstruct

Tue Sep 7 12:03:40 2004

CC three types of capsid protein VP1 (AAV58160), VP2 (AAV58161) and VP3 (AAV58162) assemble to form an icosahedral capsid, and differ from each other by the use of alternative splicing and an unusual translation initiation codon (in VP2). AAV5 capsid protein is distinct from AAV2 capsid protein and exhibits different tissue tropism. AAV2 and AAV5 are likely to utilise distinct cellular receptors and are serologically distinct. In a gene therapy application, therefore, AAV5 would allow for transduction of a patient who already possess neutralising antibodies either as a result of natural immunological defence or from prior exposure to AAV2 vectors. The vectors may be useful for transducing erythroid progenitor cells or cells lacking heparin sulphate proteoglycans, which is very inefficient with AAV2-based vectors. The vectors may also be useful for transducing cells with a nucleic acid of interest in order to produce cell lines that could be used to screen for agents that interact with the gene product of the nucleic acid of interest. In addition to transduction of other cell types, transduction of erythroid cells would be useful or the treatment of cancer and genetic diseases which can be corrected by bone marrow transplants using matched donors

XX
SQ Sequence 330 AA;
Query Match 100.0%; Score 1755; DB 3; Length 330;
Best Local Similarity 100.0%; Pred. No. 6.7e-164;
Matches 330; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MALVNLVHEGHTSEKQWIOENQESYLSFNSTGNSRSQIKALDNATKIMSLTKSAVDYL 60
DB 1 MALVNLVHEGHTSEKQWIOENQESYLSFNSTGNSRSQIKALDNATKIMSLTKSAVDYL 60

QY 61 VGSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKTNIA 120
DB 61 VGSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKTNIA 120

QY 121 EAIHTVPPFYGCNVNTNENFPDNCVDKMLIWEEGKMTNKVESAAILGSKVRVDQK 180
DB 121 EAIHTVPPFYGCNVNTNENFPDNCVDKMLIWEEGKMTNKVESAAILGSKVRVDQK 180

QY 181 CKSSVQIDSTPVIIVTSNTNMCVVVDGNSITFEHQPLEDRMFKFELTKRLPPDFGKITQ 240
DB 181 CKSSVQIDSTPVIIVTSNTNMCVVVDGNSITFEHQPLEDRMFKFELTKRLPPDFGKITQ 240

QY 241 EVKDFEAWAKVNPVTHEFKVPRELAGTKGAESLKRPLGDVNTSYKSLKRLARL 300
DB 241 EVKDFEAWAKVNPVTHEFKVPRELAGTKGAESLKRPLGDVNTSYKSLKRLARL 300

QY 301 PETPRSSDVTVDPAPLRLNWSRLVGRSW 330
DB 301 PETPRSSDVTVDPAPLRLNWSRLVGRSW 330

RESULT 2
AAU11408 standard; protein; 330 AA.
XX AAU11408
AC AAU11408;
XX
XX 26-FEB-2002 (first entry)
XX
XX Adeno-associated virus 5 (AAV5), Rep40 protein.
XX
XX Adeno-associated virus 5; AAV5; Rep40; nootropic; neuroprotective;
XX cytotatic; gene therapy; Parkinson's disease; Alzheimer's disease;
XX demyelination disease; metabolic disorder; musculoskeletal disease;
XX cardiovascular disease; cancer; autoimmune disorder; genetic disease;
XX cystic fibrosis; pseudohypocalcaemia; immunotile cilia syndrome;
XX bronchitis; pneumonia; emphysema; pulmonary oedema;
XX central nervous system; replication; transcription.
XX
XX Adeno-associated virus 5.
XX
XX WO200170276-A2.

PD 27-SEP-2001.
XX
XX 22-MAR-2001; 2001WO-US009123.
XX
XX 22-MAR-2000; 2000US-00533427.
XX
XX (IOWA) UNIV IOWA RES FOUND.
XX (USSH) US DEPT HEALTH & HUMAN SERVICES.
XX
XX Chlorini JA, Kotin RM, Davidson B, Zabner J;
XX WPI; 2002-055104/07.
XX N-PSDB; AAS17712.
XX
XX Delivering nucleic acid into cell for treating Parkinson's disease, by administering to cell an adeno-associated virus 5 particle comprising the nucleic acid inserted between a pair of AAV inverted terminal repeats.
XX
XX Disclosure; Page 125; 130pp; English.
XX
XX The invention describes a novel method of delivering a nucleic acid into a cell in a subject, comprising administering to the cell an adeno-associated virus 5 (AAV5) particle. AAV5 is a small non-pathogenic virus which relies on a helper virus for replication, in the absence of which the AAV5 genome is integrated into a host chromosome in a locus specific manner. The method provides a way to deliver a nucleic acid to a specific regions, tissues and cell types of the central nervous system comprising inserting the nucleic acid between a pair of AAV inverted terminal repeats or delivering an AAV5 particle containing a vector comprising the nucleic acid. The method is useful for treating brain disorders such as demyelination disease, Alzheimer's disease and Parkinson's disease, and metabolic disorders such as musculoskeletal diseases, cardiovascular disease, cancer and autoimmune disorders, for treating genetic diseases such as cystic fibrosis, alpha-1-antitrypsin, pseudohypocalcaemia, immunotile cilia syndrome, and for treating bronchitis, pneumonia, emphysema, and cardiogenic and non-cardiogenic pulmonary oedema. AAV5 is useful for delivering gene that may have a systematic effect like anti-hypertension drugs, insulin, coagulation factors, antibiotics, growth factors and hormones. This is the amino acid sequence of the adeno-associated virus 5 (AAV5) Rep40 protein, one of 4 Rep proteins that regulate replication and transcription of the AAV5 genome, described in the method of the invention

XX
SQ Sequence 330 AA;
Query Match 100.0%; Score 1755; DB 5; Length 330;
Best Local Similarity 100.0%; Pred. No. 6.7e-164;
Matches 330; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MALVNLVHEGHTSEKQWIOENQESYLSFNSTGNSRSQIKALDNATKIMSLTKSAVDYL 60
DB 1 MALVNLVHEGHTSEKQWIOENQESYLSFNSTGNSRSQIKALDNATKIMSLTKSAVDYL 60

QY 61 VGSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKTNIA 120
DB 61 VGSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKTNIA 120

QY 121 EAIHTVPPFYGCNVNTNENFPDNCVDKMLIWEEGKMTNKVESAAILGSKVRVDQK 180
DB 121 EAIHTVPPFYGCNVNTNENFPDNCVDKMLIWEEGKMTNKVESAAILGSKVRVDQK 180

QY 181 CKSSVQIDSTPVIIVTSNTNMCVVVDGNSITFEHQPLEDRMFKFELTKRLPPDFGKITQ 240
DB 181 CKSSVQIDSTPVIIVTSNTNMCVVVDGNSITFEHQPLEDRMFKFELTKRLPPDFGKITQ 240

QY 241 EVKDFEAWAKVNPVTHEFKVPRELAGTKGAESLKRPLGDVNTSYKSLKRLARL 300
DB 241 EVKDFEAWAKVNPVTHEFKVPRELAGTKGAESLKRPLGDVNTSYKSLKRLARL 300

QY 301 PETPRSSDVTVDPAPLRLNWSRLVGRSW 330
DB 301 PETPRSSDVTVDPAPLRLNWSRLVGRSW 330

RESULT 3	
AA558164	
ID	AA558164 standard; protein; 550 AA.
XX	
XX	AA558164;
XX	
DT	07-MAR-2000 (first entry)
XX	
DE	Adeno associated virus AAV5 Rep68 protein.
XX	
KW	Adeno associated virus; AAV5; AAV2; inverted terminal repeat; ITR;
KW	promoter; Rep protein; capsid protein; regulation; transcription;
KW	replication; chromosomal integration; tissue tropism; cellular receptor;
KW	gene therapy; neutralising antibody; erythroid progenitor cell;
KW	transduction; cancer; genetic disease; Rep68.
OS	
OS	Adeno-associated virus 5.
XX	
PN	WO9961601-A2.
XX	
PD	02-DEC-1999.
XX	
PF	28-MAY-1999; 99WO-US011958.
XX	
PR	28-MAY-1998; 98US-0087029P.
XX	
PA	(USSH) US DEPT HEALTH & HUMAN SERVICES.
XX	
PI	Chlorini JA, Kotin RM;
XX	
DR	WPI; 2000-062707/05.
DR	N-PSDB; AAZ49216.
XX	
PT	Adeno-associated virus 5 based vectors and particles, useful for gene
PT	therapy.
XX	
PS	Claim 17; Page 87-88; 91pp; English.

This sequence represents the Rep68 protein of adeno associated virus type 5 (AAV5). The invention relates to vectors comprising a pair of AAV5 inverted terminal repeats (ITRs) with a promoter between the ITRs. The vector may comprise the viral genome, or subregions thereof, including sequences encoding Rep proteins and capsid proteins, and is encapsidated in an AAV5 particle. The non-structural Rep proteins, Rep40 (AAV58613), Rep52 (AAV58168), Rep68 (AAV59164) and Rep78 (AAV59159) are involved in regulation of replication and transcription, in addition to the production of progeny genomes. Rep68 and Rep78 are also associated with the stable integration of the viral genome into human chromosomes. The three types of capsid protein VP1 (AAV58160), VP2 (AAV58161) and VP3 (AAV58162) assemble to form an icosahedral capsid, and differ from each other by the use of alternative splicing and an unusual translation initiation codon (in VP2). AAV5 capsid protein is distinct from AAV2 capsid protein and exhibits different tissue tropism. AAV2 and AAV5 are likely to utilise distinct cellular receptors and are serologically distinct. In a gene therapy application, therefore, AAV5 would allow for transduction of a patient who already possesses neutralising antibodies either as a result of natural immunological defence or from prior exposure to AAV2 vectors. The vectors may be useful for transducing erythroid progenitor cells or cells lacking heparin sulphate proteoglycans, which is very inefficient with AAV2-based vectors. The vectors may also be useful for transducing cells with a nucleic acid of interest in order to produce cell lines that could be used to screen for agents that interact with the gene product of the nucleic acid of interest. In addition to transduction of other cell types, transduction of erythroid cells would be useful or the treatment of cancer and genetic diseases which can be corrected by bone marrow transplants using matched donors.

Sequence 550 AA:

Query Match	100.0%;	Score 1755;	DB 3;	Length 550;
Best Local Similarity	100.0%;	Pred. No. 1.5e-163;		

Matches	330;	Conservative	0;	Mismatches	0;	Indels	0;	Gaps	0;
QY	1	MALVNLVVEHGTSEKQWTOENQESYLSNSTGNSRSQIKAAALDNATKIMSLTKSAVDYL	60						
Db	221	MALVNLVVEHGTSEKQWTOENQESYLSNSTGNSRSQIKAAALDNATKIMSLTKSAVDYL	280						
QY	61	VGSSVPEDISKRIWQIPFMNGYDPAYAGSILYGMQCSFNKENTVWLYGPATTKNTNIA	120						
Db	281	VGSSVPEDISKRIWQIPFMNGYDPAYAGSILYGMQCSFNKENTVWLYGPATTKNTNIA	340						
QY	121	EAIHTVIFYGCVNNTNENFPENDCVDKMLIWEEGKMTNKVVESAKAILGGSKVRVDOK	180						
Db	341	EAIHTVIFYGCVNNTNENFPENDCVDKMLIWEEGKMTNKVVESAKAILGGSKVRVDOK	400						
QY	181	CKSSVOIDSTPVI VTSNTNMCVVVDGNSITTEHQQPLEDRMPKFKELTKELPPDFGKITKQ	240						
Db	401	CKSSVOIDSTPVI VTSNTNMCVVVDGNSITTEHQQPLEDRMPKFKELTKELPPDFGKITKQ	460						
QY	241	EVKOFFAWAKVQVPVTHEFKVPRELACTKGAEKSLKRLPLGQVNTNTSYKSLEKRLRSLFV	300						
Db	461	EVKOFFAWAKVQVPVTHEFKVPRELACTKGAEKSLKRLPLGQVNTNTSYKSLEKRLRSLFV	520						
QY	301	PETPRSSDVTVDPAPLPLNWNLSLVGRSW	330						
Db	521	PETPRSSDVTVDPAPLPLNWNLSLVGRSW	550						
RESULT 4									
AAU11409									
ID	AAU11409 standard; protein; 550 AA.								
XX	AAU11409;								
DT	25-FEB-2002 (first entry)								
XX	Adeno-associated virus 5 (AAV5), Rep68 protein.								
XX	Adeno-associated virus 5; AAV5; Rep68; neurotropic; neuroprotective;								
KW	cytostatic; gene therapy; Parkinson's disease; Alzheimer's disease;								
KW	demyelination disease; metabolic disorder; musculoskeletal disease;								
KW	cardiovascular disease; cancer; autoimmune disorder; genetic disease;								
KW	cystic fibrosis; pseudohypoadosteronism; immotile cilia syndrome;								
KW	bronchitis; pneumonia; emphysema; pulmonary oedema;								
KW	central nervous system; replication; transcription.								
XX	Adeno-associated virus 5.								
OS	Adeno-associated virus 5.								
XX	WO200170276-A2.								
PN	27-SEP-2001.								
PD	22-MAR-2001; 2001WO-US009123.								
XX	22-MAR-2000; 2000US-00533427.								
PR	(IOWA) UNIV IOWA RES FOUND.								
PA	(USSH) US DEPT HEALTH & HUMAN SERVICES.								
PA	Chiorini JA, Kotin RM, Davidson B, Zabner J;								
PI	WPI; 2002-055104/07.								
DR	N-PSDB; AAS17712.								
DR	Delivering nucleic acid into cell for treating Parkinson's disease, by								
PT	administering to cell an adeno-associated virus 5 particle comprising the								
PT	nucleic acid inserted between a pair of AAV inverted terminal repeats.								
XX	Disclosure; Page 126-127; 130pp; English.								
PS	The invention describes a novel method of delivering a nucleic acid into								
XX	a cell in a subject, comprising administering to the cell an adeno-								
CC	associated virus 5 (AAV5) particle. AAV5 is a small non-pathogenic virus								
CC	which relies on a helper virus for replication, in the absence of which								

the AAV5 genome is integrated into a host chromosome in a locus specific manner. The method provides a way to deliver a nucleic acid to a specific regions, tissues and cell types of the central nervous system comprising inserting the nucleic acid between a pair of AAV inverted terminal repeats or delivering an AAV5 particle containing a vector comprising the nucleic acid. The method is useful for treating brain disorders such as demyelination disease, Alzheimer's disease and Parkinson's disease, and metabolic disorders such as musculoskeletal diseases, cardiovascular disease, cancer and autoimmune disorders, for treating genetic diseases such as cystic fibrosis, alpha-1-antitrypsin, pseudohypoadosteronism, imotile cilia syndrome, and for treating bronchitis, pneumonia, emphysema, and cardiogenic and non-cardiogenic pulmonary oedema. AAV5 is useful for delivering gene that may have a systematic effect like anti-hypertension drugs, insulin, coagulation factors, antibiotics, growth factors and hormones. This is the amino acid sequence of the adeno-associated virus 5 (AAV5) Rep8 protein, one of 4 Rep proteins that regulate replication and transcription of the AAV5 genome, described in the method of the invention

Sequence 550 AA;

Query Match 100.0%; Score 1755; DB 5; Length 550;
Best Local Similarity 100.0%; Pred. No. 1.5e-163;
Matches 330; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MALVNLVVEHGITSEKQWIEQNSYLSFNSTGNSRSQIKALDNATKIMSLTKSAVDYL 60
DB 221 MALVNLVVEHGITSEKQWIEQNSYLSFNSTGNSRSQIKALDNATKIMSLTKSAVDYL 280

QY 61 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKTNIA 120
DB 281 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKTNIA 340

QY 121 EAIHTVDFYGVNWTNENPFNDCKMLIWEEGKNTNKVVSASAKAILGSKVRVDQK 180
DB 341 EAIHTVDFYGVNWTNENPFNDCKMLIWEEGKNTNKVVSASAKAILGSKVRVDQK 400

QY 181 CKSSVQIDSTPVIWTSNTNMVVDGNSSTTFHQQLPDRMFKFELTKRLLPDPFGKITQ 240
DB 401 CKSSVQIDSTPVIWTSNTNMVVDGNSSTTFHQQLPDRMFKFELTKRLLPDPFGKITQ 460

QY 241 EVKDFFAWAKVQVPTHEFKVPRELAGTGAESKSLKRLPLGVDVNTSYKSLKRLLSFV 300
DB 461 EVKDFFAWAKVQVPTHEFKVPRELAGTGAESKSLKRLPLGVDVNTSYKSLKRLLSFV 520

QY 301 PETPRSSDVTVDPAPLRLNNSRLVGRSW 330
DB 521 PETPRSSDVTVDPAPLRLNNSRLVGRSW 550

RESULT 5
ID AAY58158 standard; protein; 390 AA.
AC AAY58158;
DT 07-MAR-2000 (first entry)
XX Adeno associated virus AAV5 Rep52 protein.
DE Adeno associated virus; AAV5; AAV2; inverted terminal repeat; ITR;
KW promoter; Rep protein; capsid protein; regulation; transcription;
KW replication; chromosomal integration; tissue tropism; cellular receptor;
KW gene therapy; neutralising antibody; erythroid progenitor cell;
KW transduction; cancer; genetic disease; Rep52.
XX Adeno-associated virus 5.
OS WO9961601-A2.
XX 02-DEC-1999.
XX 28-MAY-1999; 99WO-US011958.
PF

XX 28-MAY-1998; 98US-0087029P.
PR (USSH) US DEPT HEALTH & HUMAN SERVICES.
PA Chiorini JA, Kotin RM;
XX WPI: 2000-062707/05.
XX N-PSDB; AAZ49210.
DR Adeno-associated virus 5 based vectors and particles, useful for gene therapy.
PT Claim 14; Page 75; 91pp; English.
XX This sequence represents the Rep52 protein of adeno associated virus type 5 (AAV5). The invention relates to vectors comprising a pair of AAV5 inverted terminal repeats (ITRs) with a promoter between the ITRs. The vector may comprise the viral genome, or subregions thereof, including sequences encoding Rep proteins and capsid proteins, and is encapsidated in an AAV5 particle. The non-structural Rep proteins, Rep40 (AAY58613), Rep52 (AAY58168), Rep68 (AAY58164) and Rep78 (AAY58159) are involved in regulation of replication and transcription, in addition to the production of progeny genomes. Rep68 and Rep78 are also associated with the stable integration of the viral genome into human chromosomes. The three types of capsid protein VP1 (AAY58160), VP2 (AAY58161) and VP3 (AAY58162) assemble to form an icosahedral capsid, and differ from each other by the use of alternative splicing and an unusual translation. AAV5 capsid protein is distinct from AAV2 initiation codon (in VP2). AAV5 capsid protein is distinct from AAV2 capsid protein and exhibits different tissue tropism. AAV2 and AAV5 are likely to utilise distinct cellular receptors and are serologically distinct. In a gene therapy application, therefore, AAV5 would allow for transduction of a patient who already possesses neutralising antibodies either as a result of natural immunological defence or from prior exposure to AAV2 vectors. The vectors may be useful for transducing erythroid progenitor cells or cells lacking heparin sulphate proteoglycans, which is very inefficient with AAV2-based vectors. The vectors may also be useful for transducing cells that could be used to screen for interest in order to produce cell lines that could be used to screen for agents that interact with the gene product of other cell types, transduction interest. In addition to transduction of other cell types, transduction of erythroid cells would be useful for the treatment of cancer and genetic diseases which can be corrected by bone marrow transplants using matched donors

Sequence 390 AA;
Query Match 98.1%; Score 1721; DB 3; Length 390;
Best Local Similarity 100.0%; Pred. No. 1.9e-160;
Matches 324; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MALVNLVVEHGITSEKQWIEQNSYLSFNSTGNSRSQIKALDNATKIMSLTKSAVDYL 60
DB 1 MALVNLVVEHGITSEKQWIEQNSYLSFNSTGNSRSQIKALDNATKIMSLTKSAVDYL 60

QY 61 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKTNIA 120
DB 61 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKTNIA 120

QY 121 EAIHTVDFYGVNWTNENPFNDCKMLIWEEGKNTNKVVSASAKAILGSKVRVDQK 180
DB 121 EAIHTVDFYGVNWTNENPFNDCKMLIWEEGKNTNKVVSASAKAILGSKVRVDQK 180

QY 181 CKSSVQIDSTPVIWTSNTNMVVDGNSSTTFHQQLPDRMFKFELTKRLLPDPFGKITQ 240
DB 181 CKSSVQIDSTPVIWTSNTNMVVDGNSSTTFHQQLPDRMFKFELTKRLLPDPFGKITQ 240

QY 241 EVKDFFAWAKVQVPTHEFKVPRELAGTGAESKSLKRLPLGVDVNTSYKSLKRLLSFV 300
DB 241 EVKDFFAWAKVQVPTHEFKVPRELAGTGAESKSLKRLPLGVDVNTSYKSLKRLLSFV 300

QY 301 PETPRSSDVTVDPAPLRLNNSR 324

Db 301 PETRSSDVTVDPAPLRLNWSR 324

RESULT 6
 ID AAU11403
 AC AAU11403 standard; protein; 390 AA.
 XX AAU11403;
 DT 26-FEB-2002 (first entry)
 XX
 DE Adeno-associated virus 5 (AAV5), Rep52 protein.
 XX
 KW Adeno-associated virus 5; AAV5; Rep52; neurotropic; neuroprotective;
 KW cytostatic; gene therapy; Parkinson's disease; Alzheimer's disease;
 KW demyelination disease; metabolic disorder; musculoskeletal disease;
 KW cardiovascular disease; cancer; autoimmune disorder; genetic disease;
 KW cystic fibrosis; pseudohypoadosteronism; immotile cilia syndrome;
 KW bronchitis; pneumonia; emphysema; pulmonary oedema;
 KW central nervous system; replication; transcription.
 XX
 OS Adeno-associated virus 5.
 XX
 XX WO200170276-A2.
 PN
 XX
 PD 27-SEP-2001.
 XX
 XX 22-MAR-2001; 2001WO-US009123.
 XX
 XX 22-MAR-2000; 2000US-00533427.
 PR
 XX (IOWA) UNIV IOWA RES FOUND.
 PA (USSH) US DEPT HEALTH & HUMAN SERVICES.
 PA
 XX
 PI Chiorini JA, Kotin RM, Davidson B, Zabner J;
 XX
 XX WPI; 2002-055104/07.
 DR N-PSDB; AAS17712.
 DR
 XX
 PT Delivering nucleic acid into cell for treating Parkinson's disease, by
 PT administering to cell an adeno-associated virus 5 particle comprising the
 PT nucleic acid inserted between a pair of AAV inverted terminal repeats.
 XX
 PS Disclosure; Page 114-115; 130pp; English.
 XX
 CC The invention describes a novel method of delivering a nucleic acid into
 CC a cell in a subject, comprising administering to the cell an adeno-
 CC associated virus 5 (AAV5) particle. AAV5 is a small non-pathogenic virus
 CC which relies on a helper virus for replication, in the absence of which
 CC the AAV5 genome is integrated into a host chromosome in a locus specific
 CC manner. The method provides a way to deliver a nucleic acid to a specific
 CC regions, tissues and cell types of the central nervous system comprising
 CC inserting the nucleic acid between a pair of AAV inverted terminal
 CC repeats or delivering an AAV5 particle containing a vector comprising the
 CC nucleic acid. The method is useful for treating brain disorders such as
 CC demyelination disease, Alzheimer's disease and Parkinson's disease, and
 CC metabolic disorders such as musculoskeletal diseases, cardiovascular
 CC disease, cancer and autoimmune disorders, for treating genetic diseases
 CC such as cystic fibrosis, alpha-1-antitrypsin, pseudohypoadosteronism,
 CC immotile cilia syndrome, and for treating bronchitis, pneumonia,
 CC emphysema, and cardiogenic and non-cardiogenic pulmonary oedema. AAV5 is
 CC useful for delivering gene that may have a systematic effect like anti-
 CC hypertension drugs, insulin, coagulation factors, antibiotics, growth
 CC factors and hormones. This is the amino acid sequence of the adeno-
 CC associated virus 5 (AAV5) Rep52 protein, one of 4 Rep proteins that
 CC regulate replication and transcription of the AAV5 genome, described in
 CC the method of the invention

XX Sequence 390 AA;

Query Match

Best Local Similarity 98.1%; Score 1721; DB 5; Length 390;

Matches 324; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MALVNLVEHGITSEKQWIOENQESYLSFNSTGSRQIKKALDNATKIMSLTKSAVDYL 60
 Db |||||
 1 MALVNLVEHGITSEKQWIOENQESYLSFNSTGSRQIKKALDNATKIMSLTKSAVDYL 60
 QY 61 VGSSVEDISKRIWQIFEMNGYDPAYAGSILYGCQSRFKNKNTVWLYGPATTKNTIA 120
 Db |||||
 61 VGSSVEDISKRIWQIFEMNGYDPAYAGSILYGCQSRFKNKNTVWLYGPATTKNTIA 120
 QY 121 EAIHTVPEYGCNVNENFPENDCVCKMLIWEEGKMTNKVVSAAKILGSKVRVDQK 180
 Db |||||
 121 EAIHTVPEYGCNVNENFPENDCVCKMLIWEEGKMTNKVVSAAKILGSKVRVDQK 180
 QY 181 CKSSVQIDSTPVIIVTSNTNMVVDGNSSTTPEHQOPLDRMEKFKELTKRLPDPFGKITKQ 240
 Db |||||
 181 CKSSVQIDSTPVIIVTSNTNMVVDGNSSTTPEHQOPLDRMEKFKELTKRLPDPFGKITKQ 240
 QY 241 EVKDFFAWAKVQNPVTHEFKVPRELACTKGAESLKRPLGVDVNTSYKSLKRLSLFV 300
 Db |||||
 241 EVKDFFAWAKVQNPVTHEFKVPRELACTKGAESLKRPLGVDVNTSYKSLKRLSLFV 300
 QY 301 PETRSSDVTVDPAPLRLNWSR 324
 Db |||||
 301 PETRSSDVTVDPAPLRLNWSR 324

RESULT 7

AAV58159
 ID AAV58159 standard; protein; 610 AA.
 XX
 AC AAV58159;
 XX
 DT 07-MAR-2000 (first entry)
 XX
 DE Adeno associated virus AAV5 Rep78 protein.
 XX
 KW Adeno associated virus; AAV5; AAV2; inverted terminal repeat; ITR;
 KW promoter; Rep protein; capsid protein; regulation; transcription;
 KW replication; chromosomal integration; tissue tropism; cellular receptor;
 KW gene therapy; neutralising antibody; erythroid progenitor cell;
 KW transduction; cancer; genetic disease; Rep78.
 XX
 OS Adeno-associated virus 5.
 XX
 XX WO9961601-A2.
 PN
 XX
 PD 02-DEC-1999.
 XX
 XX 28-MAY-1999; 99WO-US011958.
 PF
 XX 28-MAY-1999; 98US-0087029P.
 PR
 XX (USSH) US DEPT HEALTH & HUMAN SERVICES.
 PA
 XX Chiorini JA, Kotin RM;
 PI
 XX WPI; 2000-062707/05.
 DR N-PSDB; AAZ49211.
 XX
 XX Adeno-associated virus 5 based vectors and particles, useful for gene
 PT therapy.
 PT
 PS Claim 15; Fig 6; 91pp; English.
 XX
 CC This sequence represents the Rep78 protein of adeno associated virus type
 CC 5 (AAV5). The invention relates to vectors comprising a pair of AAV5
 CC inverted terminal repeats (ITRs) with a promoter between the ITRs. The
 CC vector may comprise the viral genome, or subregions thereof, including
 CC sequences encoding Rep proteins and capsid proteins, and is encapsidated
 CC in an AAV5 particle. The non-structural Rep proteins Rep40 (AAV58163),
 CC Rep52 (AAV58168), Rep68 (AAV58164) and Rep78 (AAV58159) are involved in
 CC regulation of replication and transcription, in addition to the
 CC production of progeny genomes. Rep68 and Rep78 are also associated with

Tue Sep 7 12:03:40 2004

the stable integration of the viral genome into human chromosomes. The three types of capsid protein VP1 (AAV58160), VP2 (AAV58161) and VP3 (AAV58162) assemble to form an icosahedral capsid, and differ from each other by the use of alternative splicing and an unusual translation initiation codon (in VP2). AAV5 capsid protein is distinct from AAV2 capsid protein and exhibits different tissue tropism. AAV2 and AAV5 are likely to utilize distinct cellular receptors and are serologically distinct. In a gene therapy application, therefore, AAV5 would allow for transduction of a patient who already possesses neutralising antibodies either as a result of natural immunological defence or from prior exposure to AAV2 vectors. The vectors may be useful for transducing erythroid progenitor cells or cells lacking heparin sulphate proteoglycans, which is very inefficient with AAV2-based vectors. The vectors may also be useful for transducing cells with a nucleic acid of interest in order to produce cell lines that could be used to screen for agents that interact with the gene product of the nucleic acid of interest. In addition to transduction of other cell types, transduction of erythroid cells would be useful or the treatment of cancer and genetic diseases which can be corrected by bone marrow transplants using matched donors

Sequence 610 AA;
Query Match 98.1%; Score 1721; DB 3; Length 610;
Best Local Similarity 100.0%; Pred. No. 3.8e-160;
Matches 324; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
1 MALVNLVEHGITSEKQWIOENQESYLSFNSGTGNSRSQIKALDNTKIMSLTKSAVDYL 60
221 MALVNLVEHGITSEKQWIOENQESYLSFNSGTGNSRSQIKALDNTKIMSLTKSAVDYL 280
61 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKTNIA 120
281 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKTNIA 340
121 EAIHTVFPYGCNVNTNENFPNDVCDKMLIWEEGKTNKVESAKAILGSKVRVDQK 180
341 EAIHTVFPYGCNVNTNENFPNDVCDKMLIWEEGKTNKVESAKAILGSKVRVDQK 400
181 CKSSVQIDSTPVTIVTSNTNMCVVVDGNSSTTFHQOPLDRMFKFELTKRLPPDGGKITKQ 240
401 CKSSVQIDSTPVTIVTSNTNMCVVVDGNSSTTFHQOPLDRMFKFELTKRLPPDGGKITKQ 460
241 EVKDFFAWAKVQVPTHEFKVPRELAGTKGAESLKRPLGVDVNTSYKSLEKARLSFV 300
461 EVKDFFAWAKVQVPTHEFKVPRELAGTKGAESLKRPLGVDVNTSYKSLEKARLSFV 520
301 PETPRSSDVTVDPAPLPLNNSR 324
521 PETPRSSDVTVDPAPLPLNNSR 544

RESULT 8
AAV97720
ID AAV97720 standard; protein; 610 AA.
XX AAV97720;
AC AAV97720;
XX AAV97720;
DT 19-JUN-2001 (first entry)
XX Rep protein sequence.
XX Fusion nucleic acid library; Rep protein; tumour cell; apoptosis;
KW nucleic acid modification enzyme; cell death; decreased cell growth;
KW protein-protein interaction detection; cell division; cancer therapy;
KW protein drug discovery; pharmacogenetics.
XX Adeno associated virus 5.
OS Adeno associated virus 5.
XX WO200114539-A2.
XX 01-MAR-2001.
XX

18-AUG-2000; 2000WO-US022906.
20-AUG-1999; 99US-0150004P.
02-JUN-2000; 2000US-0209130P.
(UYOJ) UNIV JOHNS HOPKINS SCHOOL MEDICINE.
Li M;
WPI; 2001-218443/22.
N-PSDB; AAR91310.
New library of fusion nucleic acids each encoding a Rep protein recognized by a nucleic acid modification enzyme and a candidate protein, useful for detecting protein-protein interactions, protein drug discovery or pharmacogenetics.
Disclosure; Fig 21; 106pp; English.
This sequence is the adeno associated virus 5 Rep protein. The invention relates to a library of fusion nucleic acids, each encoding a Rep protein, a candidate protein, a presentation structure, a targeting sequence or a label. The Rep protein is a nucleic acid modification enzyme. The random or directed libraries (including the cDNA libraries) can be introduced into any tumour cell, and peptides identified which by themselves induce apoptosis, cell death, loss of cell division or decreased cell growth. The methods and compositions may also be used to detect protein-protein interactions, protein drug discovery, particularly for protein drugs that interact with targets on cell surfaces, to discover DNA or nucleic acid binding proteins, using nucleic acids as targets, to screen for nucleic acid modification enzymes with decreased toxicity for the host cells, to identify or generate Rep proteins with expression vectors and in pharmacogenetic studies. The method is useful in cancer therapy and in killing tumour cells. The methods can be combined with other cancer therapeutics (drugs or radiation) to sensitize cells and thus induce rapid and specific apoptosis, cell death, loss of cell division or decreased cell growth after exposure to a secondary agent

Sequence 610 AA;
Query Match 98.1%; Score 1721; DB 4; Length 610;
Best Local Similarity 100.0%; Pred. No. 3.8e-160;
Matches 324; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
1 MALVNLVEHGITSEKQWIOENQESYLSFNSGTGNSRSQIKALDNTKIMSLTKSAVDYL 60
221 MALVNLVEHGITSEKQWIOENQESYLSFNSGTGNSRSQIKALDNTKIMSLTKSAVDYL 280
61 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKTNIA 120
281 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKTNIA 340
121 EAIHTVFPYGCNVNTNENFPNDVCDKMLIWEEGKTNKVESAKAILGSKVRVDQK 180
341 EAIHTVFPYGCNVNTNENFPNDVCDKMLIWEEGKTNKVESAKAILGSKVRVDQK 400
181 CKSSVQIDSTPVTIVTSNTNMCVVVDGNSSTTFHQOPLDRMFKFELTKRLPPDGGKITKQ 240
401 CKSSVQIDSTPVTIVTSNTNMCVVVDGNSSTTFHQOPLDRMFKFELTKRLPPDGGKITKQ 460
241 EVKDFFAWAKVQVPTHEFKVPRELAGTKGAESLKRPLGVDVNTSYKSLEKARLSFV 300
461 EVKDFFAWAKVQVPTHEFKVPRELAGTKGAESLKRPLGVDVNTSYKSLEKARLSFV 520
301 PETPRSSDVTVDPAPLPLNNSR 324
521 PETPRSSDVTVDPAPLPLNNSR 544

RESULT 9
AAU11404

AAU11404 standard; protein; 610 AA.
 AAU11404;
 26-FEB-2002 (first entry)
 Adeno-associated virus 5 (AAV5), Rep78 protein.
 Adeno-associated virus 5; AAV5; Rep78; neurotropic; neuroprotective; cytostatic; gene therapy; Parkinson's disease; Alzheimer's disease; demyelination disease; metabolic disorder; musculoskeletal disease; cardiovascular disease; cancer; autoimmune disorder; genetic disease; cystic fibrosis; pseudohypoadosteronism; immotile cilia syndrome; bronchitis; pneumonia; emphysema; pulmonary oedema; central nervous system; replication; transcription.
 Adeno-associated virus 5.
 WO200170276-A2.
 27-SEP-2001.
 22-MAR-2001; 2001WO-US009123.
 22-MAR-2000; 2000US-00533427.
 (IOWA) UNIV IOWA RES FOUND.
 (USSH) US DEPT HEALTH & HUMAN SERVICES.
 Chiorini JA, Kotin RM, Davidson B, Zabner J;
 WPI; 2002-055104/07.
 N-PSDB; AAS17712.
 Delivering nucleic acid into cell for treating Parkinson's disease, by administering to cell an adeno-associated virus 5 particle comprising the nucleic acid inserted between a pair of AAV inverted terminal repeats.
 Disclosure; Fig 6; 130pp; English.
 The invention describes a novel method of delivering a nucleic acid into a cell in a subject, comprising administering to the cell an adeno-associated virus 5 (AAV5) particle. AAV5 is a small non-pathogenic virus which relies on a helper virus for replication, in the absence of which the AAV5 genome is integrated into a host chromosome in a locus specific manner. The method provides a way to deliver a nucleic acid to a specific regions, tissues and cell types of the central nervous system comprising inserting the nucleic acid between a pair of AAV inverted terminal repeats or delivering an AAV5 particle containing a vector comprising the nucleic acid. The method is useful for treating brain disorders such as demyelination disease, Alzheimer's disease and Parkinson's disease, and metabolic disorders such as musculoskeletal diseases, cardiovascular disease, cancer and autoimmune disorders, for treating genetic diseases such as cystic fibrosis, alpha-1-antitrypsin, pseudohypoadosteronism, immotile cilia syndrome, and for treating bronchitis, pneumonia, emphysema, and cardiogenic and non-cardiogenic pulmonary oedema. AAV5 is useful for delivering gene that may have a systematic effect like anti-hypertension drugs, insulin, coagulation factors, antibiotics, growth factors and hormones. This is the amino acid sequence of the adeno-associated virus 5 (AAV5) Rep78 protein, one of 4 Rep proteins that regulate replication and transcription of the AAV5 genome, described in the method of the invention
 Sequence 610 AA;

Query Match
 Best Local Similarity 98.1%; Score 1721; DB 5; Length 610;
 Matches 324; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 1 MALVNLVHGHTSEKQWIQENQESYLSFNSGTGNSRQIKAAALDNATKIMSLTKSAVDYL 60
 221 MALVNLVHGHTSEKQWIQENQESYLSFNSGTGNSRQIKAAALDNATKIMSLTKSAVDYL 280

QY 61 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKNTIA 120
 DB |||||
 281 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTVWLYGPATTKNTIA 340
 QY 121 EAIHTVPEYGCNNWNTNENFPNDCVDMKLIWEEGKMTNKVVSAAKILGSKVRVDQK 180
 DB |||||
 341 EAIHTVPEYGCNNWNTNENFPNDCVDMKLIWEEGKMTNKVVSAAKILGSKVRVDQK 400
 QY 181 CKSSVQIDSTPVIIVTSNTNMCVVVDGNSSTTFHQOPLDRMEKFKELTKLPDFGKITKQ 240
 DB |||||
 401 CKSSVQIDSTPVIIVTSNTNMCVVVDGNSSTTFHQOPLDRMEKFKELTKLPDFGKITKQ 460
 QY 241 EVKOFFAWAKVNPVPTHEFKVPRELACTGKAESLKRPLGVDVNTSYKSLKRLARLSFV 300
 DB |||||
 461 EVKOFFAWAKVNPVPTHEFKVPRELACTGKAESLKRPLGVDVNTSYKSLKRLARLSFV 520
 QY 301 PETPRSDVTVDPAPLRLNWSR 324
 DB |||||
 521 PETPRSDVTVDPAPLRLNWSR 544
 RESULT 10
 AAE22887
 ID AAE22887 standard; protein; 610 AA.
 XX
 AC AAE22887;
 XX
 DT 29-AUG-2003 (revised)
 DT 09-AUG-2002 (first entry)
 XX
 DE Adeno-associated virus 5 Rep protein.
 XX
 KW Nucleic acid/protein conjugate; NAP; nucleic acid modification; NAM; EAS;
 KW drug discovery; Rep protein; adeno-associated virus; AAV; gene therapy;
 KW cytostatic; Rep protein.
 XX
 OS Adeno associated virus; 5.
 XX
 FN WO200222826-A2.
 XX
 PD 21-MAR-2002.
 XX
 PF 14-SEP-2001; 2001WO-US028702.
 XX
 PR 14-SEP-2000; 2000US-0232960P.
 XX
 PA (XENC-) XENCOR INC.
 XX
 PI Li M, Melander C, Liu H;
 XX
 DR WPI; 2002-393969/42.
 DR N-PSDB; AAD36281.
 XX
 PT Library of nucleic acid/protein conjugates, has a fusion of nucleic acid
 PT modification enzyme and candidate compound, and expression vector having
 XX a fusion of nucleic acids encoding NAM enzyme and the compound.
 PS Disclosure; Fig 21; 96pp; English.
 XX
 CC The present invention relates to genetic libraries of nucleic acid/
 CC protein (NAP) conjugates comprising a fusion polypeptide (with a nucleic
 CC acid modification (NAM) enzyme (E) and candidate compound), an expression
 CC vector (with a fusion of nucleic acids encoding the enzyme and candidate
 CC protein respectively), an enzyme attachment sequence (EAS; RNA sequence),
 CC where the candidate compound and candidate protein are different and EAS
 CC and the enzyme are covalently linked. The NAP conjugates are useful in
 CC screens to assay binding to target molecules and/or to screen candidate
 CC agents for the ability to modulate the activity of the target molecule.
 CC They are useful in cancer therapy. Sequences of the invention are also
 CC useful to detect protein-protein interaction, in drug discovery, to
 CC discover DNA or nucleic acid binding proteins, using nucleic acids as the
 CC targets and to screen for NAM enzymes with decreased toxicity for host

Generating a library of fusion nucleic acids for treating cancer or infection, or detecting protein-protein interaction, comprises providing computationally-derived library of candidate protein sequences and expression vectors.

Disclosure; Page 180-182; 246pp; English.

The present invention relates to a novel method of generating a library of fusion nucleic acids. The method involves providing a computationally-derived library of candidate protein sequences and creating a library of expression vectors containing a fusion nucleic acid having a sequence encoding a nucleic acid modification (NAM) enzyme and a sequence encoding a candidate protein sequence from the library and an enzyme attachment sequence (EAS) that is recognised by the NAM enzyme. The invention also relates to the use of a variety of computation methods including protein design automation (PDA). The method is useful in generating and screening fusion nucleic acids that may be used in treating cancer or infections, in detecting protein-protein interactions, discovery of DNA or nucleic acid binding proteins, protein drug discovery, screening for NAM enzymes with decreased toxicity to the host cells and NAM enzyme/EAS pairs with increased affinity or in pharmacogenetic studies. The invention is also used in gene therapy. The present sequence is Adeno-associated virus 5 Rep protein. This sequence is used to illustrate the method of the invention. (Updated on 29-AUG-2003 to standardise OS field)

Query Match 98.1%; Score 1721; DB 5; Length 610;
Best Local Similarity 100.0%; Pred. No. 3.8e-160;
Matches 324; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

1 MALVNLVHGHTSEKOWIQENQESYLSFNSTGNSRSQIKALDNDATKIMSLTKSAVDYL 60
221 MALVNLVHGHTSEKOWIQENQESYLSFNSTGNSRSQIKALDNDATKIMSLTKSAVDYL 280
61 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTWLYGPATTKTNIA 120
281 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTWLYGPATTKTNIA 340
121 EAIHTVPFYGCNVNTNENFPFNDVCDKMLIWEEGKMTNKVESAAILGGSKVRVDOK 180
341 EAIHTVPFYGCNVNTNENFPFNDVCDKMLIWEEGKMTNKVESAAILGGSKVRVDOK 400
181 CKSSVQIDSTPVIIVTSNTNMVVDGNSSTTFHQOPLDRMPKFKLTKEPLDPFGKITKQ 240
401 CKSSVQIDSTPVIIVTSNTNMVVDGNSSTTFHQOPLDRMPKFKLTKEPLDPFGKITKQ 460
241 EVKDFPAWAKNOVPVTHEFKVPRELAGTKGAEKSLKRLPLGVDVNTSYKSLEKRLSFV 300
461 EVKDFPAWAKNOVPVTHEFKVPRELAGTKGAEKSLKRLPLGVDVNTSYKSLEKRLSFV 520
301 PETPRSSDVTVDPAPLRPLNWNRSR 324
521 PETPRSSDVTVDPAPLRPLNWNRSR 544

RESULT 12
AAE26940
ID AAE26940 standard; protein; 610 AA.
XX AC
XX AC
XX AC
13-DEC-2002 (first entry)
XX DT
XX DE
Adeno associated virus 5 Rep protein.
XX XX
Prokaryotic library; candidate protein; nucleic acid modification; NAM;
XX KW enzyme attachment sequence; EAS; clinical pharmacology; chemical sensor;
XX KW enzymology; cosmetic research; toxic; environmental safety assessment;
XX KW nutrient biology; Rep protein.
XX OS Adeno associated virus.
XX XX

cells (specifically Rep proteins with reduced toxicity). NAP conjugates are also useful in pharmacogenomic studies, for screening bioactive agents on surface cells, viruses and microbial organisms. They are also useful for screening proteins causing phenotypic changes such as overproduction or inhibition of protein expression, or proteins that alter attachment, infectivity, etc. of the virus. Sequences of the invention are also used in gene therapy. The present sequence is adeno-associated virus (AAV) 5 Rep. (Updated on 29-AUG-2003 to standardise OS field)

Sequence 610 AA;

Query Match 98.1%; Score 1721; DB 5; Length 610;
Best Local Similarity 100.0%; Pred. No. 3.8e-160;
Matches 324; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

1 MALVNLVHGHTSEKOWIQENQESYLSFNSTGNSRSQIKALDNDATKIMSLTKSAVDYL 60
221 MALVNLVHGHTSEKOWIQENQESYLSFNSTGNSRSQIKALDNDATKIMSLTKSAVDYL 280
61 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTWLYGPATTKTNIA 120
281 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTWLYGPATTKTNIA 340
121 EAIHTVPFYGCNVNTNENFPFNDVCDKMLIWEEGKMTNKVESAAILGGSKVRVDOK 180
341 EAIHTVPFYGCNVNTNENFPFNDVCDKMLIWEEGKMTNKVESAAILGGSKVRVDOK 400
181 CKSSVQIDSTPVIIVTSNTNMVVDGNSSTTFHQOPLDRMPKFKLTKEPLDPFGKITKQ 240
401 CKSSVQIDSTPVIIVTSNTNMVVDGNSSTTFHQOPLDRMPKFKLTKEPLDPFGKITKQ 460
241 EVKDFPAWAKNOVPVTHEFKVPRELAGTKGAEKSLKRLPLGVDVNTSYKSLEKRLSFV 300
461 EVKDFPAWAKNOVPVTHEFKVPRELAGTKGAEKSLKRLPLGVDVNTSYKSLEKRLSFV 520
301 PETPRSSDVTVDPAPLRPLNWNRSR 324
521 PETPRSSDVTVDPAPLRPLNWNRSR 544

RESULT 11
AAE28644
ID AAE28644 standard; protein; 610 AA.
XX AC
XX AC
XX AC
29-AUG-2003 (revised)
XX DT
XX DT
27-DEC-2002 (first entry)
XX DE
Adeno-associated virus 5 Rep protein.
XX XX
Nucleic acid modification enzyme; NAM; enzyme attachment sequence; EAS;
XX KW protein design automation; PDA; cancer; protein-protein interaction;
XX KW infection; gene therapy; Rep protein.
XX XX
Adeno associated virus; 5.
XX OS
XX WO200268453-A2.
XX PN
XX XX
06-SEP-2002.
XX PD
XX PF
19-FEB-2002; 2002WO-US004853.
XX PR
22-FEB-2001; 2001US-00792629.
XX FR
XX XX
(XENC-) XENCOR INC.
XX PA
XX XX
Li M, Dahiyat BI;
XX PI
XX WPI; 2002-691553/74.
XX DR
XX N-PSDB; AAD46138.
XX DR
XX XX

PN WO200266653-A2.
 XX 29-AUG-2002.
 XX 14-DEC-2001; 2001WO-US0490508.
 XX 14-DEC-2000; 2000US-0256163P.
 XX (XENC-) XENCOR INC.
 XX Li M, Liu Y;
 XX WPI; 2002-667068/71.
 XX N-PSDB; AAD44600.
 XX New library of prokaryotic pET-24a expression vectors, host cells or
 PT nucleic acid/protein conjugates, useful for screening candidate proteins
 PT and their nucleic acids or modification enzymes for pharmacogenetic
 PT analysis.
 XX
 XX Disclosure; Fig 21; 127pp; English.
 XX
 CC The invention relates to methods and compositions for the construction of
 CC prokaryotic libraries expressing candidate proteins and the use of these
 CC libraries to identify candidate proteins and the nucleic acids encoding
 CC them. The invention provides a library of prokaryotic pET-24a vectors
 CC comprising a fusion nucleic acid consisting of a nucleic acid encoding a
 CC nucleic acid modification (NAM) enzyme or a candidate protein, or a
 CC nucleic acid having a T7 promoter operably linked to the NAM enzyme or
 CC the candidate protein, and an enzyme attachment sequence (EAS) recognised
 CC by the NAM enzyme. The library is used for identifying candidate proteins
 CC and nucleic acids encoding these proteins, in screening for NAM enzymes
 CC with decreased toxicity for the host cells, or in identifying novel or
 CC improved EASs, which may be used for understanding cellular processes or
 CC any subsequent therapeutic or toxic activities. The nucleic acid/protein
 CC (NAP) conjugates are useful in diagnostic assays and in research
 CC including clinical pharmacology, functional genomics, pharmacogenomics,
 CC agricultural chemicals, environmental safety assessment, chemical sensor,
 CC nutrient biology, cosmetic research or enzymology. These may also be used
 CC in vitro screening techniques and in assays with target molecules. The
 CC present sequence is Adeno associated virus 5 Rep protein used in the
 CC invention
 XX
 XX Sequence 610 AA;
 SQ
 Query Match 98.1%; Score 1721; DB 5; Length 610;
 Best Local Similarity 100.0%; Pred. No. 3.8e-160;
 Matches 324; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 1 MALVNWLVHGHITSEKQWIOENQESYLSFNSTGNSRSQIKALDNATKIMSLTGSVDYL 60
 Db 221 MALVNWLVHGHITSEKQWIOENQESYLSFNSTGNSRSQIKALDNATKIMSLTGSVDYL 280
 QY 61 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTWLYGPATTGKTNIA 120
 Db 281 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTWLYGPATTGKTNIA 340
 QY 121 EAIHTVPFYGCNVNTNENFPNDCVDRKMLIWEEGKMTNKVVEAKAILGSKVRVDOK 180
 Db 341 EAIHTVPFYGCNVNTNENFPNDCVDRKMLIWEEGKMTNKVVEAKAILGSKVRVDOK 400
 QY 181 CKSSVQIDSTVITVTSNTNMCVVVDGNSTTTTEHQOPLDRMFKELTKRLPPDFGKITQ 240
 Db 401 CKSSVQIDSTVITVTSNTNMCVVVDGNSTTTTEHQOPLDRMFKELTKRLPPDFGKITQ 460
 QY 241 EVKQFFAWAKNVQPVTHFEKVPRELACTGKAESLKRPLGDVNTVNTYSKLEKARLSFV 300
 Db 461 EVKQFFAWAKNVQPVTHFEKVPRELACTGKAESLKRPLGDVNTVNTYSKLEKARLSFV 520
 QY 301 PETPRSSDVTVDPAFLPLNWSR 324
 Db 521 PETPRSSDVTVDPAFLPLNWSR 544

RESULT 13
 ABU64865
 ID ABU64865 standard; protein; 610 AA.
 XX
 AC ABU64865;
 XX
 DT 14-MAY-2003 (first entry)
 XX
 DE Rep protein sequence from adeno-associated virus 5.
 XX
 KW Rep protein; capture probe; expression vector;
 KW nucleic acid protein conjugate; NAP; enzyme attachment sequence; EAS;
 KW biochip; gene expression profiling; mutation detection; Rep68; Rep78;
 KW nonstructural protein; NS1; major coat protein; U94.
 XX
 OS Adeno-associated virus 5.
 XX
 PN US2002172968-A1.
 XX
 PD 21-NOV-2002.
 XX
 PF 19-FEB-2002; 2002US-00080376.
 XX
 PR 22-FEB-2001; 2001US-00792630.
 XX
 PA (LIUH/) LIU H.
 PA (DAHI/) DAHIYAT B I.
 PA (LITM/) LI M.
 XX
 PI Liu H, Dahiyat BI, Li M;
 XX
 DR WPI; 2003-310986/30.
 DR N-PSDB; ABX36669.
 XX
 XX New composition comprising a substrate consisting of an array of capture
 PT probes hybridized to an expression vector or to a nucleic acid protein
 PT conjugate, useful for diagnostic test, gene expression profiling or
 PT mutation detection.
 XX
 XX Disclosure; Fig 21; 125pp; English.
 XX
 CC The invention relates to a composition comprising a substrate comprising
 CC an array of capture probes hybridized to an expression vector or to a
 CC nucleic acid protein conjugate. The capture probes are hybridized to an
 CC expression vector or to a nucleic acid protein (NAP) conjugate. The
 CC vector comprises: (a) a fusion nucleic acid; (b) a capture sequence; and
 CC (c) an enzyme attachment sequence (EAS). The NAP conjugate comprises: (a)
 CC a fusion polypeptide; and (b) an expression vector. The fusion nucleic
 CC acid comprises a nucleic acid encoding the NAP enzyme or candidate
 CC protein. The fusion polypeptide comprises a Rep enzyme or candidate
 CC protein. The EAS and NAP enzyme are covalently attached. Also included are
 CC detecting the presence of a target analyte in a sample, making biochips,
 CC and making NAP conjugates. The composition is useful for diagnostic
 CC applications, gene expression profiling or mutation detection. The
 CC present sequence represents a viral Rep (or related protein e.g. Rep68,
 CC Rep78, nonstructural protein, NS1, major coat protein or U94 protein) for
 CC use in the composition of the invention
 XX
 XX Sequence 610 AA;
 SQ
 Query Match 98.1%; Score 1721; DB 6; Length 610;
 Best Local Similarity 100.0%; Pred. No. 3.8e-160;
 Matches 324; Conservative 0; Mismatches 0; Indels 0; Gaps 0;
 QY 1 MALVNWLVHGHITSEKQWIOENQESYLSFNSTGNSRSQIKALDNATKIMSLTGSVDYL 60
 Db 221 MALVNWLVHGHITSEKQWIOENQESYLSFNSTGNSRSQIKALDNATKIMSLTGSVDYL 280
 QY 61 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTWLYGPATTGKTNIA 120
 Db 281 VGSSVPEDISKRIWQIFEMNGYDPAYAGSILYGCQSFNKRNTWLYGPATTGKTNIA 340

target analyte can be nucleic acid, drug, drug analogues or prodrugs. The biochip compositions allow rapid and facile creation of protein biochips. The sequences presented in ABU64750-ABU64772 are the proteins disclosed in the invention

XX Sequence 610 AA;

Query Match 98.1%; Score 1721; DB 6; Length 610;
Best Local Similarity 100.0%; Pred. No. 3.8e-160;
Matches 324; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MALVNLVVEHGTSEKQWIOENQERSVLSFNSTGNSRSQIKAAIDNATKIMSLTKSAVDYL 60
DB 221 MALVNLVVEHGTSEKQWIOENQERSVLSFNSTGNSRSQIKAAIDNATKIMSLTKSAVDYL 280
QY 61 VGSVPEDISKRIWQIFEMNGYDYPAYAGSILYGCQSFENKENTVWLYGPATTKTNIA 120
DB 281 VGSVPEDISKRIWQIFEMNGYDYPAYAGSILYGCQSFENKENTVWLYGPATTKTNIA 340
QY 121 EAIATVPFYGCNVNTNENFPNDQVDMKLIWEEGKQTNKVESAKAILGGSKVRVDOK 180
DB 341 EAIATVPFYGCNVNTNENFPNDQVDMKLIWEEGKQTNKVESAKAILGGSKVRVDOK 400
QY 181 CKSSVQIDSTPVIIVTSNTNMVVDGNSSTFEHQPLEDRMFELTKRLPPDFGKITKQ 240
DB 401 CKSSVQIDSTPVIIVTSNTNMVVDGNSSTFEHQPLEDRMFELTKRLPPDFGKITKQ 460
QY 241 EVKDFFAWAKVNOVPVTHEPKVPRELAGTKGAESLKRPLGDVNTSYKSLEKRLSFV 300
DB 461 EVKDFFAWAKVNOVPVTHEPKVPRELAGTKGAESLKRPLGDVNTSYKSLEKRLSFV 520
QY 301 PETRSSDVTVDPAPLRLNNSR 324
DB 521 PETRSSDVTVDPAPLRLNNSR 544

RESULT 15

ABR43398
ID ABR43398 standard; protein; 610 AA.

XX ABR43398;

XX 21-JUL-2003 (first entry)

XX Adeno-associated virus 5 Rep protein SEQ ID NO:21.

XX Library; nucleic acid conjugate; protein conjugate; fusion protein;
XX nucleic acid modification enzyme; candidate protein; screening;
XX enzyme attachment sequence; detection; target analyte; DNA technology;
XX bioinformatic; identification; Adeno-associated virus.

XX Adeno-associated virus 5.
XX WO2003025154-A2.
XX 27-MAR-2003.
XX 12-MAR-2002; 2002WC-US0007466.
XX 14-SRP-2001; 2001US-00953351.
XX (XENC-) XENCOR.
XX Doberstein SK, Jin CH, Li M, Liu H, Melander C;
XX WPI; 2003-363143/34.
XX N-PSDB; ACC69245.
XX New libraries of nucleic acid/protein (NAP) conjugates or genetic
XX libraries encoding enzyme fusion proteins, useful in DNA technology and
XX bioinformatics, particularly for identifying genes, proteins or analytes.
XX Disclosure; Fig 21; 113pp; English.

QY 121 EAIATVPFYGCNVNTNENFPNDQVDMKLIWEEGKQTNKVESAKAILGGSKVRVDOK 180
DB 341 EAIATVPFYGCNVNTNENFPNDQVDMKLIWEEGKQTNKVESAKAILGGSKVRVDOK 400
QY 181 CKSSVQIDSTPVIIVTSNTNMVVDGNSSTFEHQPLEDRMFELTKRLPPDFGKITKQ 240
DB 401 CKSSVQIDSTPVIIVTSNTNMVVDGNSSTFEHQPLEDRMFELTKRLPPDFGKITKQ 460
QY 241 EVKDFFAWAKVNOVPVTHEPKVPRELAGTKGAESLKRPLGDVNTSYKSLEKRLSFV 300
DB 461 EVKDFFAWAKVNOVPVTHEPKVPRELAGTKGAESLKRPLGDVNTSYKSLEKRLSFV 520
QY 301 PETRSSDVTVDPAPLRLNNSR 324
DB 521 PETRSSDVTVDPAPLRLNNSR 544

RESULT 14

ABU64760
ID ABU64760 standard; protein; 610 AA.

XX ABU64760;

XX 14-MAY-2003 (first entry)

XX Adeno associated virus a Rep protein, #2.

XX Biochip; capture probe; nucleic acid modification enzyme; NAM;
XX enzyme attachment sequence; EAS; single-nucleotide polymorphism; SNP;
XX protein-protein interaction.

XX Adeno associated virus 5.

XX US2002168640-A1.

XX 14-NOV-2002.

XX 22-FEB-2001; 2001US-00792630.

XX 22-FEB-2001; 2001US-00792630.

XX (LIW//) LI M.
XX (DAH//) DAHIYAT B I.

XX Li M, Dahiyat B I;

XX WPI; 2003-298722/29.
XX N-PSDB; ABX96524.

XX Biochip composition useful for creating protein biochips for detecting
XX target analyte in a sample, has substrate having array of capture probes
XX hybridized to nucleic acid/protein conjugate.

XX Disclosure; Fig 21; 123pp; English.

XX The invention discloses a biochip composition comprising a substrate
XX having an array of capture probes, which are hybridized to a nucleic acid
XX (NA)/protein (NAP) conjugate containing a fusion polypeptide, comprising
XX a NA modification (NAM) enzyme and a candidate protein, and an expression
XX vector, comprising a NA encoding NAM enzyme and a candidate protein
XX fusion, a capture sequence and enzyme attachment sequence (EAS). The
XX biochip composition is useful for detecting the presence of a target
XX analyte in a sample, by contacting the sample with a biochip comprising
XX the compositions under conditions where target analytes can bind to at
XX least one of the candidate proteins to form an assay complex and
XX detecting the presence of target analyte on the substrate. The target
XX analyte is labelled with a fluorescent label and the method further
XX comprises adding a labelled soluble binding ligand to the assay complex.
XX The biochip compositions are useful for creating protein biochips which
XX are useful in diagnosing (detecting the presence of specific target
XX analytes), screening (looking for target analytes that bind to specific
XX proteins), and single-nucleotide polymorphism (SNP) analysis. The bioassay
XX chips are used in assays to determine protein-protein interactions. The

XX The present invention describes a library of nucleic acid/protein (NAP)
CC conjugates each comprising: (a) a fusion polypeptide comprising: (i) a
CC nucleic acid modification (NAM) enzyme; and (ii) a candidate protein; (b)
CC an expression vector having a fusion nucleic acid comprising a nucleic
CC acid encoding: (i) the NAM enzyme; and (ii) the candidate protein, where
CC at least two of the candidate proteins are different; and (c) an enzyme
CC attachment sequence (EAS), which is an RNA sequence. The EAS and the NAM
CC enzyme are covalently attached. Also described: (1) a library of
CC expression vectors; (2) making a library of fusion polypeptides; (3)
CC detecting the presence of a target analyte in a sample; and (4) screening
CC a library of small molecules. The library of NAP conjugates is useful for
CC detecting the presence of a target analyte in a sample, or for screening
CC a library of small molecules. The library is useful in DNA technology and
CC bioinformatics, particularly for identifying nucleic acids, proteins, or
CC their sequences, in their native cellular environment. The present
CC sequence represents the Adeno-associated virus 5 Rep protein, which is
CC given in the exemplification of the present invention
XX
SQ Sequence 610 AA;

Query Match 98.1%; Score 1721; DB 6; Length 610;
Best Local Similarity 100.0%; Pred. No. 3.8e-160;
Matches 324; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 MALVNLVVEHGITSEKOWIQENQESYLSFNSGTGNSRSQIKAAALDNATKIMSLTKSAVDYL 60
Db |||||
QY 221 MALVNLVVEHGITSEKOWIQENQESYLSFNSGTGNSRSQIKAAALDNATKIMSLTKSAVDYL 280
Db |||||
QY 61 VGSVPEDISKRIWQIFEMNGYDPAYAGSTLYGCQCSFNKRNVTWLYGPATTKTNIA 120
Db |||||
QY 281 VGSVPEDISKRIWQIFEMNGYDPAYAGSTLYGCQCSFNKRNVTWLYGPATTKTNIA 340
Db |||||
QY 121 EATAHTVPFYGCNVNWTNENPFNDVCDKMLIWEEGKMTNKVBSAKAILGGSKVRVDQK 180
Db |||||
QY 341 EATAHTVPFYGCNVNWTNENPFNDVCDKMLIWEEGKMTNKVBSAKAILGGSKVRVDQK 400
Db |||||
QY 181 CKSSVQIDSTPVIIVTSNTNMVVDGNSITFEHQOPLDRMFKFELTKRLPPDFGKITKQ 240
Db |||||
QY 401 CKSSVQIDSTPVIIVTSNTNMVVDGNSITFEHQOPLDRMFKFELTKRLPPDFGKITKQ 460
Db |||||
QY 241 EVKDFFAWAKVQVPVTHFKVPRELAKTGAEKSLKRLPLGDVTNTSYKSLEKRLSfv 300
Db |||||
QY 461 EVKDFFAWAKVQVPVTHFKVPRELAKTGAEKSLKRLPLGDVTNTSYKSLEKRLSfv 520
Db |||||
QY 301 PETPRSSDVTVDPAPLRLNWSR 324
Db |||||
QY 521 PETPRSSDVTVDPAPLRLNWSR 544

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